A "therapeutic gene" is one whose gene product performs a clinically useful function. For example, where the therapeutic gene is used to transform cancer cells, the therapeutic gene will inhibit the growth of the cancer cells. The therapeutic gene is preferably one whose gene product has low toxicity to non-target tissues, and high toxicity to the disease (*e.g.* cancer) site. For example, when delivered in the preferred lipid-nucleic acid (*e.g.*, lipid-plasmid particles) particles of the invention, the gene product preferably has greater toxicity to tumor cells than liver or spleen cells, where a large portion of particles can normally be cleared. Alternatively, a therapeutic gene may be delivered to a treatment site, which is not a disease site, but which activates an immunologic or other response which is then favorable for the amelioration of the disease or disorder being treated. Examples of therapeutic genes useful in the methods of the present invention include, but are not limited to, genes for: pro-apoptotic proteins; tumor suppressors (*e.g.*, p53, Rb1 (Retinoblastoma), *etc.*); cytokines (such as Interleukin-2, Interleukin-12, *etc.*); heat shock proteins; immunogenic antigens (such as tumor-specific proteins, *etc.*); genes activated in embryos only; Endostatin, Angiostatin, Thrombospondin, and other inhibitors of angiogenesis; Enzymes used in Gene Directed Enzyme Prodrug Therapy ("GDEPT") combinations (*i.e.*, suicide genes used in conjunction with a non-toxic pro-drug), such as Thymidine Kinase from Herpes simplex virus (HSV-TK); cytosine deaminase; porfirin; TIMP-2 (tissue inhibitor of metallo proteinase-2); plant, bacterial or fungal toxin genes, such as saporin, ricin, diphtheria toxin, cholera toxin; viral protein genes, such as E1A; mutated E6; SV40 Tag or viral protein genes which effect plasmid maintenance and/or copy number, such as EBNA-1; transcription plasmids encoding ribozymes or antisense oligonucleotides, Adenosine Deaminase; CFTR - Cystic Fibrosis; GM-CSF, IL-4, IL-2, IL-7, IL-10; Carcineombryonic Antigen; HLA-B7; TNF; T-Cell Receptor Antibody; CEA; Ig; IFN-g; MART-1; Chimeric Antibody/TCR; Prostate Specific Antigen; anti-erbB-2; Single Chain Antibody; BRCA-1; Alpha-1 Antitrypsin; p47 phax; Fanconi Anemia Complementation Group C; Glucocerbrosidase; Iduronato-2-Sulfatase; Purine Nulceaside Phosphorylase. Other therapeutic genes are continually being discovered and can be used in the methods of